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Practitioner's Docket No. MPI01-019P1RNM ***PATENT***

In re application of:	Curtis, Rory A.J.		
Application No.:	10/074,547	Group No.:	1647
Filed:	February 12, 2002	Examiner:	Kapust, Rachel B.
For:	25466, A HUMAN TRANSPORTER FAMILY MEMBER AND USES THEREFOR		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.131

Sir:

I, Rory A.J. Curtis, hereby declare and state:

1. I am the inventor of the subject matter described and claimed in the above-identified application.

2. I was in possession of the complete nucleic acid sequence of 25466 in the United States and had determined its identity as a monocarboxylate transporter before January 30, 2001.

3. Evidence is provided by the following:
a) Prior to January 30, 2001, I had completed the sequencing of full length human 25466. Exhibit A is a copy of an electronic printout of the nucleic acid sequence from Millennium's sequence database. The printout bears the automatically embedded date on which I entered the sequence into the database. On the original printout, this sequence bears a date prior to January 30, 2001. In accordance with accepted practice, the dates on the copy of the electronic printout have been masked (M.P.E.P. § 715.07).

The top sections of the printout bear reference information for accessing the 25466

CERTIFICATION UNDER 37 C.F.R. SECTIONS 1.8(a) and 1.10*

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☑ deposited with the United States Postal Service in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
37 C.F.R. SECTION 1.8(a)

☑ with sufficient postage as first class mail.

37 C.F.R. SECTION 1.10*

☐ as "Express Mail Post Office to Addressee" Mailing Label No.

TRANSMISSION

☐ transmitted by facsimile to the Patent and Trademark Office.

Signature

Sean Hunziker/Beverly Sotiropoulos

Date: July 8, 2004

(type or print name of person certifying)

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sequence in the Millennium database. The remainder of the printout bears the entire 25466 nucleotide sequence ("Fbh25466pat"), known in the application as SEQ ID NO:1.

b) Prior to January 30, 2001, I had determined that the 25466 nucleotide sequence of SEQ ID NO:1 encodes a monocarboxylate transporter based on the results of analyses of the nucleotide sequence and the encoded polypeptide. Exhibits B, C and D are evidence of this determination. Exhibit B is a copy of the first page of a BLAST analysis of SEQ ID NO:1. The top hit in this BLAST result is human monocarboxylate transporter 3 (Genbank Accession No. U81800). Exhibit C is a copy of several analyses of the 25466 polypeptide, with the sequence displayed on page 1. Page 4 of Exhibit C shows the alignment of a portion of the polypeptide with the MCT (monocarboxylate transporter) domain in Pfam. Exhibit D is a pairwise alignment of the 25466 polypeptide with human monocarboxylate transporter 4 (SwissProt Accession No. O15374). I performed my analyses and reached the conclusion that SEQ ID NO:1 encodes a monocarboxylate transporter prior to January 30, 2001.

The original printouts of Exhibits B and C bear automatically embedded dates on which I performed these analyses. In accordance with accepted practice, the dates on the copies of the electronic printouts have been masked (M.P.E.P. § 715.07).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Rory Curtis

Rory A.J. Curtis

6/12/2004

Date

Exhibit A to Accompany Declaration under 37 CFR §1.131 for US Appln. No. 10/074,547

Sample Information

name: Fbh25466pat
type: Plain DNA Sequence
submitted on:
NC project: Bayer
species: Human
tissue: unspecified
internal id: 107698647
restrictions: none

Sequences Information

creation method: Loading
name: Load
created on:
created by: Rory Curtis
accession number: 107698648

> Fbh25466pat - Import - complete

```
1       GTCGACCCAC GCGTCCGCAA GAGTGTGCAT GTGAGGTGAC TGCATTTTTT TTCCCTGCCA
61      AACCAGAATT AGCCGGTATA GGAATGAACG AGCATGAAGA TTTGAAATTG CTCCGATTGG
121     AAGGAAGCCC AGGTTAGGTT TGGGCACCTC CAAACGCACC CGTTTTAAAG CCACCTGGAC
181     TGAGGCGTCG AGCTTTCAGC TCCACCAAAC GCTCACCTGG CCTGGCAGCG AGCGGCGGAA
241     GAGCCCGGGA GCCCCTCACA GAGCGCACCG AGCCGGGCGG AGAGCTGAGC CGCAGGCACC
301     CGCGTCTCCA GGATGATAGG CGACATTGCA ACAAATCTCT ACACCCAGCA GCTCAGGGGG
361     CTCCAAGCAG AGCAGCAAGT TCGAGGATCC GGGCGTGGAG CCGAGTGAGG CCGCAGCCCA
421     GCGGGCCTCG GGCGAAAAAT CTTGGAAAAT GTATACCAGT CATGAAGATA TTGGGTATGA
481     TTTTGAAGAT GGCCCCAAAG ACAAAAAGAC ACTGAAGCCC CACCCAAACA TTGATGGCGG
541     ATGGGCTTGG ATGATGGTGC TCTCCTCTTT CTTTGTGCAC ATCCTCATCA TGGGCTCCCA
601     GATGGCCCTG GGTGTCCTCA ACGTGGAATG GCTGGAAGAA TTCCACCAGA GCCGCGGCCT
661     GACCGCCTGG GTCAGCTCCC TCAGCATGGG CATCACCTTG ATAGTGGGCC CTTTCATCGG
721     CTTGTTCATT AACACCTGTG GGTGCCGCCA GACTGCGATC ATTGGAGGGC TCGTCAACTC
781     CCTGGGCTGG GTGTTGAGTG CCTATGCTGC AAACGTGCAT TATCTCTTCA TTACTTTTGG
841     AGTCGCAGCT GGCCTGGGCA GCGGGATGGC CTACCTGCCA GCGGTGGTCA TGGTGGGCAG
901     GTATTTCCAG AAGAGACGCG CCCTCGCCCA GGGCCTCAGC ACCACGGGGA CCGGATTCGG
961     TACGTTCCTA ATGACTGTGC TGCTGAAGTA CCTGTGCGCA GAGTACGGCT GGAGGAATGC
1021    CATGTTGATC CAAGGTGCCG TTTCCCTAAA CCTGTGTGTT TGTGGGGCGC TCATGAGGCC
1081    CCTCTCTCCT GGTAAAAACC CAAACGACCC AGGAGAGAAA GATGTGCGTG GCCTGCCAGC
1141    GCACTCCACA GAATCTGTGA AGTCAACTGG ACAGCAGGGA AGAACAGAAG AGAAGGATGG
1201    TGGGCTCGGG AACGAGGAGA CCCTCTGCGA CCTGCAAGCC CAGGAGTGCC CCGATCAGGC
1261    CGGGCACAGG AAGAACATGT GTGCCCTCCG GATTCTGAAG ACTGTCAGCT GGCTCACCAT
1321    GAGAGTCAGG AAGGGCTTCG AGGACTGGTA TTCGGGCTAC TTTGGGACAG CCTCTCTATT
1381    TACAAATCGA ATGTTTGTAG CCTTTATTTT CTGGGCTTTG TTTGCATACA GCAGCTTTGT
1441    CATCCCCTTC ATTCACCTCC CAGAAATCGT CAATTTGTAT AACTTATCGG AGCAAAACGA
1501    CGTTTTCCCT CTGACGTCAA TTATAGCAAT AGTTCACATC TTTGGAAAAG TGATCCTGGG
```

1561 CGTCATAGCC GACTTGCCTT GCATTAGTGT TTGGAATGTC TTCCTGTTGG CCAACTTCAC
1621 CCTTGTCCTC AGTATTTTTA TTCTGCCGTT GATGCACACG TACGCTGGCC TGGCGGTCAT
1681 CTGTGCGCTG ATAGGGTTTT CCAGTGGTTA TTTCTCCCTA ATGCCCGTAG TGACTGAAGA
1741 CTTGGTTGGC ATTGAACACC TGGCCAATGC CTACGGCATC ATCATCTGTG CTAATGGCAT
1801 CTCTGCATTG CTGGGACCAC CTTTTGCAGG GTGGATCTAT GACATCACGC AAAAATATGA
1861 TTTTTCCTTC TACATATGTG GTTTGCTTTA CATGATAGGA ATACTCTTTT TACTTATTCA
1921 GCCGTGCATT CGAATTATAG AACAATCCAG AAGAAAATAC ATGGATGGTG CACATGTTTA
1981 GTATCATGTA ATGTTCCGTG TAGGTTTCAT TGTAATACTC ATGCCTACCT CGCATGGTTG
2041 CTGTGAGGCA CCTATGACAG GACGTGGGAA AGCATTTTGT ACGGTAACTG GCACTGTCAT
2101 TTGTAAATGC CATTGTCACA GCCTCATTTG TAAGCAGCAC TGCCTCTCTG TTTGGGGAGA
2161 TGTAATGCTG GAAGATCTTA AGGACTACAT ACATTCTAGA GATGACAGTG TTGTTCAAAG
2221 ACAGCCTAGT AAGTAATTGG TAGAAATGCC CTTATAAAAA CCATTCTCTT GTCATCTACT
2281 GGGACTAGGG TTTTAAATAC AGCTTTTAAA AACAAAAACA GGGAATAAAA GCTTTTCAAC
2341 TCAACCACTT CTTTGTAAGA CAAAACTGAA GTATCTGTGT GCTTCCAGAA AGCTTACAGA
2401 TAAATGGGTT TCAAGCACAA GAATATGACT AGATTTCAGA AATTAATTAT TACAGGGAGC
2461 TATTGATCTA CTAGCATCAA ACAAAGGCAA GCTCTAATTC CACAGGTAAT ACAATTTAGT
2521 GCAATTAAAG AAACACGGCT TGTATTTTTA TGAGGGAATT CTGCAGCTAG GGATTGTGAC
2581 TCCTAAATCC TCCTCTAAAA GAAGGCACTT GCCATTAATC CTAATTCAGT GCTATCCAGT
2641 TATAAATGGA ATCTTGAGAC AAAACCTTAA CAAAGAAATA ACAGTAATGA TTTCCTTAGC
2701 AGAAGCCGTA TTTGTACGCA CAACATTAAA TCAAGGGCTA CAATTCAAGC ACTTTTATTC
2761 GTATCATTGG CCTCTTAGAT GATATAAGCA TGAGGTGGGG CCTGTAATAT TTTTTTCTGA
2821 GTTTCTTCTG CCCAAAAATA TAATATAGAA CTAATTGCTA ACTGACAAAT AAAGTTAATA
2881 GTTAAATCAT CTCCAAGGAA TGTTGCTAAT CCAAAGTATA ACACTATCAA TTTGTGAGGA
2941 TAATAAATGG AATGCCATTA GTGTAGATGT CTGTGCCACA TCTGACACTG GAGTAGTGAT
3001 AACAAATAGC CCATCTCTAG ACTCTCGTGT TGTTATATAG ACCATTCATT TGCCTGAGCG
3061 TGGCACAGTT TTAAAAATAG TTCTCTTGAT TGATTTCATA CAGAAGATGA CTGTGATCCA
3121 TGACATCTAA TAATGCCCTT TCTTTATCTG AGATGTCTAT TTTTCTAAGC CAAACGTTTT
3181 TCAGACTGCA GAATGTTCTT CCCAGATCAT TTGAAATTTC TGGCTGCCTT ACTTGTTTAC
3241 AGATAGTTTA AGACTATTTA AATTTCTACT CACAATTTGA TCATCACACA CACACAAATC
3301 CTTGAATATC ATTGCCAGTG TCTTAGGTCA AATTTACCTA AAGTGAATAC AGCCCATTCT
3361 CAATTATCCT TCACAATTAG ACGCAGGAAT GCTACTAGGA ATTGGAATCA AACAATGCCA
3421 CCCCAAGCGT AATTTTAGCC AGCAGTTTCA GTTATACTCA ACCATGTCCT TCTGAGCTGT
3481 TAACAAGTGA TTCAATGGAC AAGTTCTCTT TTTGTTCCAT CTCCATTATT TCCTGCTCTA
3541 ATGTATAGTG GGAGTGGTTG TGTAATGAAA GGACCACCAA AATAATAAAA GGCAGCTAAT
3601 GGAAAGGAGA GACAAAAGCA TGGTTAATAT ATATACTTAA TATTACCTCC AATGACTCGG
3661 GAATTGCCTG TAAATTATTA TAGACAATAG ATTGCATGTC ATACTCCATT TGGTTCAACA
3721 CAACAACCTA TGTGTTATCA TTACAGCTTT GGCTGCTGTT AAAGAATCCA GCTCTCTATT
3781 TTGATAAAGA TAATCTTAAA GCTGAGGCAA TGCTCCCTCC CCTATCTCTC TCTGTGTAAT
3841 TTACCATAGA ATTAGGATGA TTAGATTGAA ACACATGTTG TATGTTTTAA AAACTACATT
3901 GCTTCATTAC TTTCATTTTC CGACAACATC AAACTAACAA GAGGCAGTGT TAAATATTTT
3961 AAATGGTGCT ATAGCCAATG TATTTGAATG CTTGCACTGC TGGTTGTGTA TCATCAATAT
4021 GAACTTTTTA TCCAATGACT CAACTCTAAT TACATCTAAG TTAGACTTGC TCACGTTCAG
4081 TTTGTACAGT TGTGTGTTGA CTTACTATGT TTTGAAAGTG GTGACTTCTA CCGAATGAGT
4141 GGAAGTTCCC ATTGTCAAAA AAAATAAAGA CCTGCTTGCA GTATTCATGT TGACAACAGA
4201 GTAAAAGAGA ATACTGTAAA GAATTACTGC AAATATTTCC TGTTTATGTT ATTTGCCGTT
4261 GTTTGAAGAT ATTATAAAGG GTTAATTGTA TATTTATATC ATGTGCTTTA TCGTTTTCCC
4321 CTCATGTATC CAAGTAATTT TTATTTACAT ACAACTAAAT AAATGTTGTC CTCTTTGAAA

4381 AAAAAAAAAA AAAAAAAAAA AAAAAAAAGG GGCGGCCGC

Exhibit B to Accompany Declaration under 37 CFR §1.131 for US Appln. No. 10/074,547

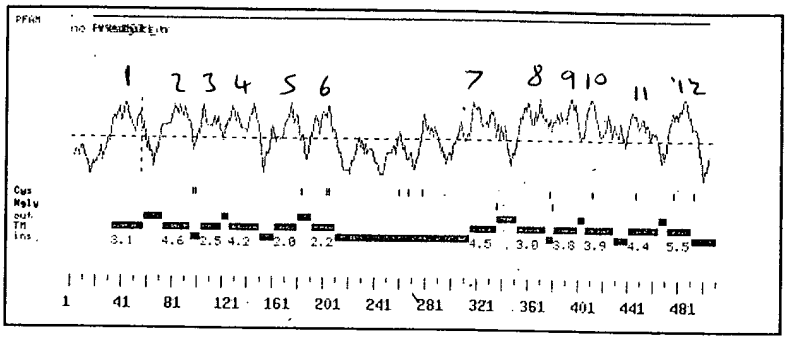
Fbh25466pat(4419 bases) -
Nucleic Acid Db Check - All Database Hits

```
gb|U81800|HSU81800 Homo sapiens monocarboxylate transport...   384  8.4e-20   1
gb|U15685|GGU15685 Gallus gallus retinal epithelial membr...   376  4.0e-19   1
gb|AJ238706|DME238706 Drosophila melanogaster mRNA for ca...   292  3.9e-12   1
gb|AF178954|AF178954 Mus musculus monocarboxylate transpo...   280  4.0e-11   1
gb|AL009193|DMC103B4 Drosophila melanogaster cosmid clone...   292  2.4e-10   2
gb|AE003423|AE003423 Drosophila melanogaster genomic scaf...   292  1.3e-09   2
gb|AE003469|AE003469 Drosophila melanogaster genomic scaf...   271  3.5e-09   2
gb|AR083262|AR083262 Sequence 9 from patent US 5976837.        231  4.9e-07   1
>gb|U81800|HSU81800 Homo sapiens monocarboxylate transporter (MCT3) mRNA,
           complete cds.
           Length = 1982

  Plus Strand HSPs:

 Score = 384 (108.6 bits), Expect = 8.4e-20, P = 8.4e-20
 Identities = 288/552 (52%), Positives = 288/552 (52%), Strand = Plus / Plus

Query:   532 TGATGGCGGATGGGCTTGGATGATGGTGCTCTCCTCTTTCTTTGTGCACATCCTCATCAT 591
             ||| ||||| ||||  |||    || |  ||  || |||| |  |      | ||  |
Sbjct:   110 TGACGGCGGCTGGGGCTGGGCCGTGCTCTTCGGCTGTTTCGTCATCACTGGCTTCTCCTA 169

Query:   592 GGGCTCCCAGATGGCCCTGGGTGTCCTCAACGTGGAATGGCTGGAAGAATTCCACCAGAG 651
              | ||  ||  | |||| |  ||||| ||  |  |||     |  | || ||        |
Sbjct:   170 CGCCTTCCCCAAGGCCGTCAGTGTCTTCTTCAAGGAGCTCATACAGGAGTTTGGGATCGG 229

Query:   652 CCGCGGCCTGACCGCCTGGGTCAGCTCCCTCAGCATGGGCATCACCTTGATAGTGGGCCC 711
             |  | ||   || ||||||  ||  |||| ||    ||| |||   ||        || ||
Sbjct:   230 CTACAGCGACACAGCCTGGATCTCCTCCATCCTGCTGGCCATGCTCTACGGGACAGGTCC 289

Query:   712 TTTCATCGGCTTGTTCATTAACACCTGTGGGTGCCGCCAGACTGCGATCATTGGAGGGCT 771
               ||  | |  ||| | | |||  || ||| |||||  |       | |  | || || ||
Sbjct:   290 GCTCTGCAGTGTGTGCGTGAACCGCTTTGGCTGCCGGCCCGTCATGCTTGTGGGGGGTCT 349

Query:   772 CGTCAACTCCCTGGGCTGGGTGTTGAGTGCCTATGCTGCAAACGTGCATTATCTCTTCAT 831
              | |    || ||||||  ||||       ||| |      | | |     |  ||| | |
Sbjct:   350 CTTTGCGTCGCTGGGCATGGTGGCTGCGTCCTTTTGCCGGAGCATCATCCAGGTCTACCT 409

Query:   832 TACTTTTGGAGTCGCAGCTGGCCTGGGCAGCGGGATGGCCTACCTGCCAGCGGTGGTCAT 891
              ||   ||| |||    | ||  ||||    |   |   || || |||  || |  ||||
Sbjct:   410 CACCACTGGGGTCATCACGGGGTTGGGTTTGGCACTCAACTTCCAGCCCTCGCTCATCAT 469

Query:   892 GGTGGGCAGGTATTTCCAGAAGAGACGCGCCCTCGCCCAGGGCCTCAGCACCACGGGGAC 951
              | ||  | | || |||   ||| | ||| || | ||| | || ||     |  | || |
Sbjct:   470 GCTGAACCGCTACTTCAGCAAGCGGCGCCCCATGGCCAACGGGCTGGCGGCAGCAGGTAG 529
```

Exhibit C to Accompany Declaration under 37 CFR §1.131 for US Appln. No. 10/074,547

Back to orfanal.cgi

Analysis of 25466 (510 aa)



No Signal Sequence
12 Transmembrane Domains
Cytoplasmic N- and C-terminals

```
>25466
MYTSHEDIGYDPEDGPKDKKTLKPHPNIDGGWAWMMVLSSFFVHILIMGSQMALGVLNVE
WLEEPHQSRGLTAWVSSLSMGITLIVGPFIGLPINTCGCRQTAIIGGLVNSLGWVLSAYA
ANVHYLPITFGVAAGLGSGMAYLPAVVMVGRYFQKRRALAQGLSTTGTGPGTFLMTVLLK
YLCAEYGWRNAMLIQGAVSLNLCVCGALMRPLSPGKNPNDPGEKDVRGLPAHSTESVKST
GQQGRTEEKDGGLGNEETLCDLQAQECPDQAGHRKNMCALRILKTVSWLTMRVRKGFEDW
YSGYFGTASLFTNRMFVAFIPWALPAYSSFVIPPIHLPEIVNLYNLSEQNDVFPLTSIIA
IVHIPGKVILGVIADLPCISVWNVFLLANFTLVLSIPILPLMHTYAGLAVICALIGFSSG
YFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWIYDITQKYDFSFYICGLL
YMIGILFLLIQPCIRIIEQSRRKYMDGAHV
```

PSORT Prediction of Protein Localization

```
MITDISC: discrimination of mitochondrial targeting seq
      R content:       0       Hyd Moment(75):   6.27
      Hyd Moment(95):  6.41    G content:        0
      D/E content:     2       S/T content:      2
      Score: -6.39

Gavel: prediction of cleavage sites for mitochondrial preseq
      cleavage site motif not found

NUCDISC: discrimination of nuclear localization signals
      pat4: none
      pat7: PKDKKTL (5) at   16
      bipartite: none
      content of basic residues:   6.5%
      NLS Score: -0.04

Final Results (k = 9/23):

         66.7 %: endoplasmic reticulum
         22.2 %: mitochondrial
         11.1 %: nuclear

 prediction for 25466 is end (k=9)
```

Start	End	Feature	Seq
387	408	Leucine zipper pattern (PS00029)	LANFTLVLSI...LPLMHTYAGL

Signal Peptide Predictions for 25466

Method	Predict	Score	Mat@
SignalP (eukaryote)	MAYBE		56

NO

Note: amino-terminal 70aa used for signal peptide prediction

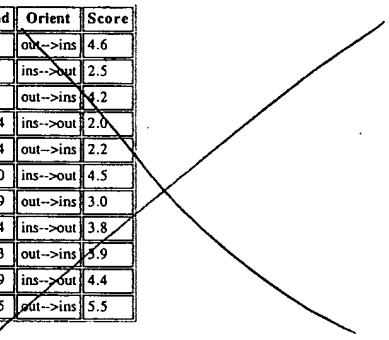
Transmembrane Segments Predicted by MEMSAT

Start	End	Orient	Score	
33	57	ins-->out	3.1	TM1
73	94	out-->ins	4.6	TM2
103	119	ins-->out	2.5	TM3
126	149	out-->ins	4.2	TM4
162	179	ins-->out	2.0	TM5
191	209	out-->ins	2.2	TM6
315	335	ins-->out	4.5	TM7
352	374	out-->ins	3.0	TM8
381	399	ins-->out	3.8	TM9
406	428	out-->ins	3.9	TM10
441	464	ins-->out	4.4	TM11
472	490	out-->ins	5.5	TM12

>25466
MYTSHEDIGYDPEDGPKDKKTLKPHPNIDGGWAWGSVLSSFFVHILIWGSQWALGVLNVE
WLSEFHQSRGLTAWVSSLSWGITLIVGPFIGLFINTCGCRQTAIIGGLVWSLGWVLSAYA
ANVHYLFITFGVAAGLGSGWAYLPAVQMVGRYFQKRRALAQGLSTTGTGFGTFLMTVLLK
YLCAEYGWRNAMLIQGAVSLNLCVCGALMRPLSPGKNPNDPGEKDVRGLPAHSTESVKST
GQQGRTEEKDGGLGNEETLCDLQAQECPDQAGHRKNMCALRILKTVSWLTMRVRKGFEDW
YSGYFGTASLFTNRMFVAFIFMALFAYSSFVIPFIHLPEIVNLYNLSEQNDVFPLTSIIA
IVHIFGKVILGVIADLPCISVWNVFLLANFTLVLSIFILPLMHTYAGLAVICALIGFSSG
YFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWIYDITQKYDFSFYICGLL
YMIGILFLLIQPCIRIIEQSRRKYMDGAHV

Transmembrane segments for presumed mature peptide

Start	End	Orient	Score
18	39	out-->ins	4.6
48	64	ins-->out	2.5
71	94	out-->ins	4.2
107	124	ins-->out	2.0
136	154	out-->ins	2.2
260	280	ins-->out	4.5
297	319	out-->ins	3.0
326	344	ins-->out	3.8
351	373	out-->ins	3.9
386	409	ins-->out	4.4
417	435	out-->ins	5.5



>25466_mature
VLNVEWLSEFHQSRGLTAWVSSLSWGITLIVGPFIGLFINTCGCRQTAIIGGLVWSLGWV
LSAYAANVHYLFITFGVAAGLGSGWAYLPAVQNVGRYFQKRRALAQGLSTTGTGFGTFLM
TVLLKYLCAEYGWRNAMLIQGAVSLNLCVCGALMRPLSPGKNPNDPGEKDVRGLPAHSTE
SVKSTGQQGRTEEKDGGLGNEETLCDLQAQECPDQAGHRKNMCALRILKTVSWLTMRVRK
GFEDWYSGYFGTASLFTNRMFVAFIFMALFAYSSFVIPFIHLPEIVNLYNLSEQNDVFPL
TSIIATVHIFGKVILGVIADLPCISVWNVFLLANFTLVLSIFILPLMHTYAGLAVICALI
GFSSGYFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWIYDITQKYDFSFY
ICGLLYMIGILFLLIQPCIRIIEQSRRKYMDGAHV

Prosite Pattern Matches for 25466

Prosite version: Release 12.2 of February 1995

>PS00001|PDOC00001|ASN_GLYCOSYLATION N-glycosylation site.

Query: 345 NLSE 348

Query: 389 NFTL 392

>PS00005|PDOC00005|PKC_PHOSPHO_SITE Protein kinase C phosphorylation site.

Query: 21 TLK 23

Query: 236 SVK 238

Query: 290 TMR 292

Query: 312 TNR 314

Query: 467 TQK 469

Query: 500 SRR 502

>PS00006|PDOC00006|CK2_PHOSPHO_SITE Casein kinase II phosphorylation site.

Query: 3 TSHE 6

Query: 258 TLCD 261

>PS00007|PDOC00007|TYR_PHOSPHO_SITE Tyrosine kinase phosphorylation site.

Query: 294 RKGFEDWY 301

>PS00008|PDOC00008|MYRISTYL N-myristoylation site.

Query: 49 GSQMAL 54

Query: 91 GLFINT 96

Query: 98 GCRQTA 103

Query: 106 GGLVNS 111

Query: 131 GVAAGL 136

Query: 137 GSGMAY 142

Query: 162 GLSTTG 167

Query: 251 GGLGNE 256

Query: 443 GIIICA 448

>PS00029|PDOC00029|LEUCINE_ZIPPER Leucine zipper pattern.

Query: 387 LANFTLVLSIFILPLMHTYAGL 408

>PS00342|PDOC00299|MICROBODIES_CTER Microbodies C-terminal targeting signal.

Query: 508 AHV 510

Protein Family / Domain Matches, HMMer version 2

```
Searching for complete domains in PFAM
hmmpfam - search a single seq against HMM database
HMMER 2.1.1 (Dec 1998)
Copyright (C) 1992-1998 Washington University School of Medicine
HMMER is freely distributed under the GNU General Public License (GPL).
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
HMM file:                 /prod/ddm/seqanal/PFAM/pfam5.5/Pfam
Sequence file:            /prod/ddm/wspace/orfanal/oa-script.8673.seq
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
 Query:   25466
```

Scores for sequence family classification (score includes all domains):

Model	Description	Score	E-value	N
MCT	Monocarboxylate transporter	184.0	2.5e-51	1
sugar_tr	Sugar (and other) transporter	-142.8	0.086	1
Presenilin	Presenilin	-256.3	4.8	1

Parsed for domains:

Model	Domain	seq-f	seq-t	hmm-f	hmm-t	score	E-value
Presenilin	1/1	17	336 ..	1	475 []	-256.3	4.8
MCT	1/1	40	477 ..	1	611 []	184.0	2.5e-51
sugar_tr	1/1	32	504 ..	1	487 []	-142.8	0.086

Alignments of top-scoring domains:

Presenilin: domain 1 of 1, from 17 to 336: score -256.3, E = 4.8

```
                *->eeelklkY.....gakhvimlfvPVslCMllVvatiks.vsfyeqnd
                   +   +lk +++ +g+    m++ +     l   + + ++v + e
       25466    17  KDKKTLKPhpnidGGWAWMMVLSSFPVHILIMGSQMALgVLNVEWLE 63

                   glkllYtpPhsdtptvgqklldSllNtlilIsVlvvmTfLlvvlYkyrFY
                   +       Ph        ++l +   +l +   l+v  f++++     ++
       25466    64 E-------FHQ------SRGLTAWVSSLSMGITLIVGPPIGLFINTCGCR 100

                   K..iIhgWLilSSlllLFlfsviyLqevfkaynDQDDNNQvp......md
                    + iI.g  +++Sl+  +   +  ++ +f ++         v+ + +++m
       25466   101 QtaIIGG--LVNSLGWVLSAYAANVHYLFITFG-------VAaglgagMA 141

                   yptvllliwnPGvvGmmciHWkgpLrLqQfYLItisa....LmAlvfiky
                   y+ +++ ++ +           +   + L Q+    t   + ++ Lm +  +ky
       25466   142 YLPAVVMVGRY---------FQKRRALAQGLSTTGTfgttfLMTVL-LKY 181

                   LPeWTaWfvLaaISvWDLVAVLtPkGPLrmLVETAqeRnepiFPAliYSS
                   L     W                          mL   A   n ++  Al+
       25466   182 LCAEYGWRN-------------------AMLIQGAVSLNLCVCGALMRPL 212

                   tvvvltvgsnqeetnegtpsterrtskstIEYyTkReaQDDEFYQKIRQR
                   +   + ++   e    g p  +  ++kst
       25466   213 SPGKNPND-PGEKDVRGLPAHSTESVKST---------------------- 240

                   rsaanPdsaptshstlVEAEPSpielkekssteeesddesdsseteGmPL
                                          +   + ++e+ d++   e++   L
```

```
       25466   241 ------------------------GQ--QGRTEEKDGGLGNEETLCDL 262

                   vsgsSNLsssdssttvsqsdsllaphr.teeiareqpevqsnslpsNekr
                    +                  q+    a hr+   +   r   +++v+    l+
       25466   263 QA--------------QECPDQAGHRknMCALRILKTVS--WLTM---- 291

                   eeTAaDalhPdGeeErgvkLGLGDFiFYSvLvGkAsatasGdwnTtIACF
                                      v+ G+ D    YS    G As           t    F
       25466   292 ---------------RVRKGFED--WYSGYFGTASLF-------TNRMF 316

                   VatLiGLclTLlllavfkkALPALPisitfGlIFYFstdilvtPFmd<-*
                   Va                  i+ +l+ Y    +  +v PF
       25466   317 VAF-----------------------IFWALFAY---SSFVIPFIH    336

MCT: domain 1 of 1, from 40 to 477: score 184.0, E = 2.5e-51
                   *->sflingftdgfpksfgliffrelqeefqasnsetswdsisSillavl
                      sf++++ v+g + + g ++ +e++eef+ s++ t+w  +sS+ ++ +
       25466    40    SFFVHILIMGSQMALG-VLNVEWLEEFHQSRGLTAW--VSSLSMGIT 83

                   lfaGPlasilvnrfGcRlvtiaGgllassgmvlasFatniselyltfGvi
                   l++GP++  + n  GcR++ i+Ggl+ s+g vl+  a n+  l +tfGv
       25466    84 LIVGPFIGLFINTCGCRQTAIIGGLVNSLGWVLSAYAANVHYLFITFGVA 133

                   tGlGfafiylPaiviitsYFekkRsLAtgiavaGsgvgtfvlaplnpdqf
                    GlG ++ ylPa+v+++ YF+k+R+LA g++++G+g+gtf+ ++l+  ++
       25466   134 AGLGSGMAYLPAVVMVGRYFQKRRALAQGLSTTGTGPGTFLMTVLL--KY 181

                   lienyGskWrgallffggmgyviAiwsvaivlncciagalfrplpsekvk
                   l + yG  Wr+a+l+ g+              + ln+c++gal+rpl ++k
       25466   182 LCAEYG--WRNAMLIQGA-----------VSLNLCVCGALMRPLSPGK-- 216

                   qtklakaeepkealkskeneaseSidsirsaakaivspetpalslspelt
                              +p
       25466   217 --------NP---------------------------------------- 218

                   ptkdqlqkllktsrtrssngakllidfsvlkdargfllyassgslaslgtq
                                              ++++ + +  l  +s++s+ s g+q
       25466   219 ------------------------NDPGEKDVRGLPAHSTESVKSTGQQ 243

                   lflpgsiflvnfakslgeslssvkskeaafllsilgdssdkegfggifar
                   + ++          k+ g      +   e+   l+      d+ g ++++ +
       25466   244 GRTE--------EKDGG-----LGNEETLCDLQAQ-ECPDQAGHRKNMCA 279

                   patllsflgfvanlketksnrpvliyllslcsivavvingilsrlasala
                   + +        + + ++    +  +++  ++                ++   +
       25466   280 LRI-------LKTVSW---LTMRVRKGFE-------------DWYSGYFG 306

                   gsrkekkiksmidkielkstfwglflfslffgvgfgskkavvilalgfll
                   +                          + lf ++ f+ ++f        ++a++ +
       25466   307 T-------------------ASLFTNRMFVAFIFW-----ALFAYSSFV 331

                   fsilyaipvvglqkyssalGltetdAstlieaiavlniiGrplaGllaDk
                    +++   + +v l ++g+    ++       l+++ia++ i G +++G +aD
       25466   332 IPFIHLPEIVNLYNLSEQNDVF-----PLTSIIAIVHIPGKVILGVIADL 376

                   tknrklaiynlslilcGlfvafaPlatiflglafycvlfGsivfllayaF
                   + ++    ++ l+   ++l+++++Pl +++ gla++c+l
       25466   377 PCISVWNVFLLANFTLVLSIFILPLMHTYAGLAVICALI---------- 415

                   kgfckgsyialtsviavdltgldklsnafgllllfqGvatlvGppiagll
                    gf+ g y++l+++v+++dl+g + l na+g+++ + G+ +l Gpp+ag++
       25466   416 -GFSSG-YFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWI 463

                   kdltgsykvafyfa<-*
                   +d+t+ y+ sfy++
       25466   464 YDITQKYDFSFYIC    477

sugar_tr: domain 1 of 1, from 32 to 504: score -142.8, E = 0.086
                   *->valvaalgGgflfGyDtgviggflalidflfrfglltssqalaelgy
                      +a++ +l +    ++    +i g ++ + +l  ++l +  ++ ++
       25466    32    WAWMMVLSS----FFVHILIMGSQMALGVLNVEWLEEFHQSRGL--- 71

                   stvltglvvaifflGrliGslfaGklgdrfGRkksllialvlfviGalls
                      t++w s  +   li + f G +++  G + + +i++++ + G +ls
       25466    72 ----TAWVSSLSMGITLIVGPFIGLFINTCGCRQTAIIGGLVNSLGWVLS 117

                   gaapgytTiGlwafyllivGRvlvGlgvGgasvlvPmYisEiAPkalRGa
                   + a +       +yl+i + v +Glg G a+  + + ++       +R a
       25466   118 AYAANV-------HYLFITFGVAAGLGSGMAYLPAVVMVGRY--FQKRRA 158

                   lgslyqlaitiGilvAaiiglglnktnndsalnswgWRiplglqlvpall
                   l+  + l++t+  + ++++++ l++  +     + gWR  + +q++ +l
       25466   159 LA--QGLSTTGTGFGTFLMTVLLKYLCA-----EYGWRNAMLIQGAVSLN 201

                   lligllflP.........................ESPRwLvekgkleeAre
                   l++++ + ++ ++++++++++++ ++ + +++ES    +  +g++ee +
       25466   202 LCVCGALMRplspgknpndpgekdvrglpahstESVKSTGQQGRTEEKDG 251

                   vLak...lrgv.................edvdqeiqeikaeleagveee.k
                    L  +++l+  + ++ +++ +++++  ++ +++ + + + ++  +  e
       25466   252 GLGNeetLCDLqaqecpdqaghrknmcALRILKTVSWLTMRVRKGFEDwY 301

                   agkaswgelfrgrtrpkvrqrllmgvmlqafqQltGiNaifYYsptifks
                    g    ++lf++         r+++++  +a+  ++     f   p i +
       25466   302 SGYFGTASLFTN--------RMFVAFIFWALFAYSSFVIPFIHLPEIVNL 343

                   ........vGvsdsrasllvtiivgvvNfvfTlvalifIvDrfGRRplli
                    + ++++v   +s    ++ i++ +  ++  ++a ++ + ++   + +l
       25466   344 ynlseqndVPPLTS----IIAIVHIPGKVILGVIADLPCISVW---NVPL 386

                   lGaagmaicflilgasigvallllnkpkdplskaagivaivfillfiafP
                   l  +++++  +il         +l ++          +++a+ ++l+    F
       25466   387 LANFTLVLSIPIL--------PLMHTY--------AGLAVICALIG---F 417

                   alqwGpipwvilsElFPtkvRskalalataanwlanfiigflfpyitgai
                     g+  ++ v++ +l   +  + a ++  +an +++ + + ++ +i +

                                                    http://tango.mpi.com/seqanal/orfanal/25466.8670.html
```

```
      25466   418 SSGYFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWIYDIT 467

                  glalggyvflvfaglllvlfilfvfffvPETKGrtLeeieelf<-*
                        y f ++  + +l  + ++f+++  ++r +e+  + +
      25466   468 Q----KYDFSFYI-CGLLYMIGILFLLIQPCIRIIEQSRRKY    504

//
Searching for complete domains in SMART
hmmpfam - search a single seq against HMM database
HMMER 2.1.1 (Dec 1998)
Copyright (C) 1992-1998 Washington University School of Medicine
HMMER is freely distributed under the GNU General Public License (GPL).
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
HMM file:                 /ddm/robison/smart/smart/smart.all.hmms
Sequence file:            /prod/ddm/wspace/orfanal/oa-script.8673.seq
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
 Query:   25466

Scores for sequence family classification (score includes all domains):
Model    Description                                       Score    E-value  N
-------- -----------                                       -----    ------- ---
        [no hits above thresholds]

Parsed for domains:
Model    Domain  seq-f seq-t    hmm-f hmm-t      score  E-value
-------- ------- ----- -----    ----- -----      -----  -------
        [no hits above thresholds]

Alignments of top-scoring domains:
        [no hits above thresholds]
//
```

ProDom Matches

ProdomId	Start	End	Description	Score
View Prodom 38068 [Boxer] [Showing match] [Go!]	345	461	p99.2 (2) O06142(1) O30820(1) // PROTEIN ADENYLYL CYCLASE	73
View Prodom 102799 [Boxer] [Showing match] [Go!]	393	467	p99.2 (1) YU45_MYCTU // HYPOTHETICAL 41.9 KD PROTEIN CY339.45C TRANSMEMBRANE	80
View Prodom 84838 [Boxer] [Showing match] [Go!]	440	494	p99.2 (1) Q23113_CAEEL // SIMILAR TO SYNAPTIC VESICLE AMINE TRANSPORTER	74
ProdomId	Start	End	Description	Score

View Prodom 84838

```
>84838 p99.2 (1) Q23113_CAEEL // SIMILAR TO SYNAPTIC VESICLE AMINE TRANSPORTER
        Length = 85

 Score = 74 (31.1 bits), Expect = 0.053, P = 0.052
 Identities = 18/57 (31%), Positives = 31/57 (54%)

Query:    440 NAYGIIICANGISALLGPPFAGWIYDITQKYDFSFYICGLLYMI--GILFLLIQPCI 494
              +   GI +     +  L+GPP+ G +Y  + K +  F +  LL +     I P+++QP I
Sbjct:     14 SAMGIALGGLALGVLVGPPYGGLLYQWSGK-ELPFVLLALLALFDGSIQFMVLQPKI 69
```

View Prodom 102799

```
>102799 p99.2 (1) YU45_MYCTU // HYPOTHETICAL 41.9 KD PROTEIN CY339.45C
        TRANSMEMBRANE
        Length = 155

 Score = 80 (33.2 bits), Expect = 0.55, P = 0.43
 Identities = 25/78 (32%), Positives = 37/78 (47%)

Query:    393 VLSIFILPLMHT-YAGLAVICALI-GFSSGYF-SLMPVVTEDLVGIEHLANAYGIIICAN 449
              +LSI ++     T    + VI  L+ G + G    S +  V  DLV      A+AYG+
Sbjct:     48 ILSILVVLFAPTDNVTMVVIGTLVWGAAVGIQESTLRGVVADLVASPRRASAYGVFAAGL 107

Query:    450 GISALLGPPFAGWIYDIT 467
              G +   G     GW+YDI+
Sbjct:    108 GAATAGGGALIGWLYDIS 125
```

View Prodom 38068

```
>38068 p99.2 (2) O06142(1) O30820(1)  // PROTEIN ADENYLYL CYCLASE
        Length = 218

 Score = 73 (30.8 bits), Expect = 8.1, P = 1.0
```

Identities = 41/135 (30%), Positives = 62/135 (45%)

```
Query:   345 NLSEQNDVFPLTSIIAIVHI--FGKVILGVIADLPCISVWNVFLLANPTLV--LSIP--- 397
             +++ +  V  +T+ +A+V    F  + L   A    I++ NVF    F +V  L  F
Sbjct:    15 SVARRQRVLTITAWLAVVVTGSFALMQLATGAGGWYIALINVFTAVTFAIVPLLHRFGGL 74

Query:   398 ILPLMHTYAGLAVICAL-IGPSSG-------YFSLMPVVTEDLVGIEHLANAYGIIICAN 449
             + PL  T+ G A +    IG+  G       +F +   +   LVGIEH A A G+   A
Sbjct:    75 VAPL--TFIGTAYVAIFAIGWDVGTDAGAQFFFLVAAALVVLLVGIEHTALAVGLAAVAA 132

Query:   450 G-ISAL--LGPPFAG 461
             G + AL  L PP  G
Sbjct:   133 GLVIALEFLVPPDTG 147
```

Exhibit D to Accompany Declaration under 37 CFR §1.131 for US Appln. No. 10/074,547

```
CLUSTAL W (1.74) multiple sequence alignment

Fbh25466pat     MYTSHEDIGYDFEDGPKDKKTLKPHPNIDGGWAWMMVLSSFFVHILIMGSQMALGVLNVE
O15374          --------MLKRE-GKVQPYT----KTLDGGWGWMIVIHFFLVNVFVMGMTKTFAIFFVV
                         . * *  :  *     .:****.**:*:  *:*::::**   ::.:: *

Fbh25466pat     WLEEFHQSRGLTAWVSSLSMGITLIVGPFIGLFINTCGCRQTAIIGGLVNSLGWVLSAYA
O15374          FQEEFEGTSEQIGWIGSIMSSLRFCAGPLVAIICDILGEKTTSILGAFVVTGGYLISSWA
                : ***. :    .*:.*:  .: : .**::.:: :  * : *:*:*.:* : *:::*::*

Fbh25466pat     ANVHYLFITFGVXAGLGSGMAYLPAVXMVGRYFQKRRALAQGLSTTGTGFGTFLMTVLLK
O15374          TSIPFLCVTMGLLPGLGSAFLYQVAAVVTTKYFKKRLALSTAIARSGMGL-TFLLAPFTK
                :.: :* :*:*: .****.: *  *. :. :**:** **: .:: :* *: ***:: : *

Fbh25466pat     YLCAEYGWRNAMLIQGAVSLNLCVCGALMRPLSPGKNPNDPGEKDVRG-LPAHSTESVKS
O15374          FLIDLYDWTGALILFGAIALNLVPSSMLLRPI-HIKSENNSGIKDKGSSLSAHGPEAHAT
                :*   *.* .*::: **::***  .. *:**:   *. *:.* **  . *.**..*:  :

Fbh25466pat     TGQQGRTEE---KDG---GLGNE-ETLCDLQAQECPDQAGHRKNMCALRILKTVSWLTMR
O15374          ETHCHETEESTIKDSTTQKAGLPSKNLTVSQNQSEEFYNGPNRN----RLLLKSDEESDK
                  :  .***   **.     *   :.*   * *.     * .:*    *:* . .  : :

Fbh25466pat     VRKGFEDWYSGYFGTASLFTNRMFVAFIFWA-LFAYSSFVIPFIHLPEIVNLYNLSEQND
O15374          VIS----WSCKQLFDISLFRNPFFYIFT-WSFLLSQLAYFIPTFHLVARAKTLGID-IMD
                * .    * .  :   *** * :*  *  *: *::  ::.** :**   .:  .:.   *

Fbh25466pat     VFPLTSIIAIVHIFGKVILGVIADLPCISVWNVFLLANFTLVLSIFILPLMHTYAGLA--
O15374          ASYLVSVAGILETVSQIISGWVADQNWIKKYHYHKSYLILCGITNLLAPLATTFPLLMTY
                .  *.*: .*:. ..::* * :**   *. :: .    :   :: :: **  *:. *

Fbh25466pat     VICALIGFSSGYFSLMPVVTEDLVGIEHLANAYGIIICANGISALLGPPFAGWIYDITQK
O15374          TICFAI-FAGGYLALILPVLVDLCRNSTVNRFLGLASFFAGMAVLSGPPIAGWLYDYTQT
                .**  * *:.**::*:  *  **   . : .  *:     *::.* ***:***:** **.

Fbh25466pat     YDFSFYICGLLYMIGILFLLIQPCIRIIEQSRRKYMDGAHV
O15374          YNGSFYFSGICYLLSSVSFFFVP---LAERWKNSLT-----
                *: ***:.*: *::. : ::: *   : *: :..
```